

10/049,874

1-23

147,19-23 vector species #3-6 surface
1,2,3 overall

WO 01/12235

18 method

PCT/US00/22619

② Linker 19-23

WHAT IS CLAIMED IS

1. A non-naturally occurring viral gene therapy vector for cell-specific delivery of nucleic acid to a target cell, comprising a recombinant viral core, a non-naturally occurring functional surface moiety, and a linker that associates said recombinant core with said functional surface moiety,

5 wherein said core comprises a nucleic acid molecule;
wherein said vector promotes production of at least one therapeutic nucleic acid, peptide, or protein;

10 wherein said functional surface moiety comprises at least one functional element selected from the group consisting of an immunoprotective element, a targeting element, and a cell-entry element; and

wherein said linker comprises at least one element selected from the group consisting of a multivalent polymer and a polymer-modified lipid; and

whereby said vector binds to and delivers said core into a target cell.

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2. The vector according to claim 1, wherein said core further comprises at least one viral capsid protein.

20 3. The vector according to claim 1, wherein said functional surface moiety comprises an immunoprotective element.

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4. The vector according to claim 1, wherein said functional surface moiety comprises a targeting element.

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25 5. The vector according to claim 1, wherein said functional surface moiety comprises a cell-entry element.

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6. The vector according to claim 1, wherein said functional surface moiety comprises an immunoprotective element, a targeting element, and a cell-entry element.

5 7. The vector according to claim 3, wherein said immunoprotective element is a synthetic polymer moiety.

8. The vector according to claim 4, wherein said targeting moiety binds to a receptor that is more highly expressed in diseased cells than in normal cells.

10 9. The vector according to claim 8, wherein said targeting moiety is a peptide or peptidomimetic ligand for a cell surface receptor.

15 10. The vector according to claim 5, wherein said cell-entry element is a membrane-destabilizing moiety.

11. The vector according to claim 10, wherein said membrane-destabilizing moiety comprises an amphiphilic α -helix.

20 12. The vector according to claim 10, wherein said membrane-destabilizing moiety comprises a copolymer of glutamic acid with leucine.

13. The vector according to claim 11, wherein said amphiphilic α -helix is derived from the C-terminal domain of a viral *env* protein.

14. The vector according to claim 13, wherein C-terminal domain is the C-terminal domain of the Moloney leukemia virus *env* protein.

15. The vector according to claim 14, wherein said C-terminal domain 5 comprises amino acids 598-616 of the Moloney leukemia virus *env* protein.

16. The vector according to claim 7, wherein said synthetic polymer component comprises a poly(ethyleneglycol).

10 17. The vector according to claim 7, wherein said synthetic polymer component comprises a copolymer of glutamic acid with leucine.

18. A method of treating a disease in a patient, comprising administering to said patient a therapeutically effective amount of a vector according to claim 1.

15 19. The gene therapy vector of claim 1, wherein said linker comprises a multivalent polymer.

20. The gene therapy vector of claim 19, wherein said multivalent polymer consists essentially of glutamic acid and leucine amino acids.

21. The gene therapy vector of claim 1, wherein said linker comprises a polymer-modified lipid.

22. The gene therapy vector of claim 21, wherein the proximal end of said poly-modified lipid is modified with a hydrophobic or amphiphilic moiety.

23. The gene therapy vector of claim 21, wherein the distal end of said 5 polymer-modified lipid is modified with a ligand or targeting moiety.